COPY FOR IB

Rec'd PCT/PTO 24 SEP 2004

PATENT COOPERATION TREATY

REC'D 04 JUN 2004

WIPO PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. **PCT/KR2003/000593**	International filing date *(day/month/year)* **25 MARCH 2003 (25.03.2003)**	Priority date *(day/month/year)* 25 MARCH 2002 (25.03.2002)

International Patent Classification (IPC) or national classification and IPC

IPC7 A61K 31/661

Applicant

BioSynergen, Inc. et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
25 OCTOBER 2003 (25.10.2003)	24 MAY 2004 (24.05.2004)

Name and mailing address of the IPEA/KR

Korean Intellectual Property Office
920 Dunsan-dong, Seo-gu, Daejeon 302-701,
Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

LEE, Mi Jeong

Telephone No. 82-42-481-5601

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International aplication No.
PCT/KR2003/000593

I. Basis of the report

1. With regard to the elements of the international application:*

- [X] the international application as originally filed
- [ ] the description:
  pages _____, as originally filed
  pages _____, filed with the demand
  pages _____, filed with the letter of _____
- [ ] the claims:
  pages _____, as originally filed
  pages _____, as amended (together with any statment) under Article 19
  pages _____, filed with the demand
  pages _____, filed with the letter of _____
- [ ] the drawings:
  pages _____, as originally filed
  pages _____, filed with the demand
  pages _____, filed with the letter of _____
- [ ] the sequence listing part of the description:
  pages _____, as originally filed
  pages _____, filed with the demand
  pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language English which is

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [X] the language of publication of the international application(under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide** and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- [X] contained inthe international application in written form.
- [X] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disc losure in the international applicationas as filed has been furinshed.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages _____
   - [ ] the claims, Nos. _____
   - [ ] the drawings, sheet _____

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box(Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed." and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 - 25	YES
	Claims		NO
Inventive step (IS)	Claims	1 - 25	YES
	Claims		NO
Industrial applicability (IA)	Claims	20 - 25	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents have been considered for the purpose of this report:

D1: Science, Vol. 293(5530), pp. 618-619 (2001)
D2: J. Am. Soc. Nephrol., Vol. 12, pp. 456-463 (2001)

1. Novelty

The subject-matter of claims 1-25 in the present invention relates to methods for treating inflammatory diseases associated with neutrophil accumulation and hyperactivity and/or excessive release of IL-8, by administering LPC (lysophosphatidylcholine) or SPC (sphingophosphorylcholine). The description of the present invention includes experimental data showing 1) the inhibitory effects of LPC and SPC against the anti-apoptosis of neutrophils by inflammation mediators, 2) the inhibitory effects of LPC against the release of IL-8 produced by macrophages, and 3) the improved therapeutic effects of LPC in bacteria-induced sepsis model.

D1 discloses that LPC may nonspecifically recruit T cells to sites of tissue damage, but then, high levels of LPC may serve to put the brakes on further T cell activation. D2 discloses that atherosclerosis is a chronic inflammatory disease associated with enhanced apoptotic cell death in vascular cells and that LPC dose-dependently induced apoptosis of human endothelial cells.

None of the prior art discloses that LPC can induce neutrophil apoptosis, inhibit the release of IL-8, and increase the bactericidal activity of neutrophils. Therefore, the subject-matter of claims 1-25 can be considered novel [Article 33(2) PCT].

2. Inventive Step

Even though D1 and D2 are relevant to the present invention in terms of dealing with the relationship between LPC and inflammation, there is no indication that the teachings of D1 and D2 would have led those skilled in the art to use LPC or SPC to induce neutrophil apoptosis, to inhibit the release of IL-8, and to increase the bactericidal activity of neutrophils.
(Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of:

Box V

Therefore, an inventive step can be acknowledged for the subject-matter of claims 1-25 [Art 33(3) PCT].

3. Industrial Applicability

The subject-matter of claims 1-19 relates to a method of therapeutic treatment. Concerning the assessment of the industrial applicability of the subject-matter relating to therapeutic applications, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims [Article 33(4) PCT].